Remarks

Reconsideration of this Application is respectfully requested.

I. Status of the Claims

Upon entry of the foregoing amendment, claims 1-30 are pending in the application, with claim 1 being the independent claim. Claims 1, 2, 3, 5, 7, 9, 10, and 11 are sought to be amended. Support for the amendment to claim 1 can be found throughout the as-filed specification. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

II. Rejection of Claims 1-30 Under 35 U.S.C. § 102(b)

The Examiner has maintained the rejection of claims 1-30 under 35 U.S.C. § 102(b) as allegedly being anticipated by "Binz et al 1990 Eur. J. Biochem. 189:73-8." (Office Action, page 3, lines 1-3). Applicants respectfully traverse this rejection.

Applicants note that the citation to "Binz et al 1990 Eur. J. Biochem. 189:73-8" is incorrect. It is believed that the Examiner intended to cite Binz, T., *et al., J. Bio. Chem. 265*:9153-9158 (1990)(hereinafter "Binz"), a copy of which was provided by the Examiner in the Office Action mailed June 5, 2008, in the present application.

The Examiner alleges that "[t]he claims do not recite any closed claim language such that additional amino acids must be excluded. Moreover, the limitations of the

claim allow for the full length molecule, because the claim is drawn to a fragment or variant thereof, i.e., the full length molecule is a 'variant' of the claimed molecule which lacks a functional C-terminal." (Office Action, page 3, lines 14-18). Applicants respectfully disagree.

However, in furtherance of prosecution, claim 1 has been amended. Applicants have amended claim 1 to recite that the single chain polypeptide, the fragment of the single chain polypeptide, or the variant of the single chain polypeptide lacks a functional C-terminal part of a clostridial neurotoxin heavy chain designated H_C thereby rendering the polypeptide, fragment, or variant incapable of binding to cell surface receptors that are the natural cell surface receptors to which native clostridial neurotoxin binds.

Binz discloses a full length BoNT/A holotoxin which comprises a *functional* C-terminal part of a clostridial neurotoxin heavy chain designated H_C. Conversely, claim 1 expressly excludes a full-length BoNT/A holotoxin with a *functional* C-terminal part of a clostridial neurotoxin heavy chain designated H_C. Claim 1 recites that the single chain polypeptide, the fragment of the single chain polypeptide, or the variant of the single chain polypeptide *lacks a functional* C-terminal part of a clostridial neurotoxin heavy chain designated H_C. The feature "lacks a functional C-terminal part of a clostridial neurotoxin heavy chain designated H_C" is essential to parts (I), (II), and (III) of claim 1. Parts (I), (II), and (III) of claim 1 cannot comprise a *functional* C-terminal part of a clostridial neurotoxin heavy chain designated H_C and therefore, claim 1 is not anticipated by Binz.

Accordingly, Applicants respectfully submit that the rejection of claims 1-30 under 35 U.S.C.§102(b) has been obviated, and should be withdrawn.

III. Rejection of Claims 1-29 Under Nonstatutory Obviousness-Type Double Patenting

The Examiner has provisionally rejected claims 1-29 based on nonstatutory obviousness-type double patenting as alleged being unpatentable over claims 1-14, 16-32, 34, 37-39, and 54 of copending U.S. Appl. No. 11/644,010 to Shone *et al.* (Office Action, page 4, lines 1-3)[1]. Applicants respectfully traverse the rejection.

Applicants respectfully request that the currently asserted double patenting rejection be held in abeyance until claimed subject matter is otherwise deemed allowable. After analyzing the final allowed claim scope, Applicants will consider filing a terminal disclaimer if necessary to overcome any obviousness-type double patenting rejections.

IV. Rejection of Claims 1-3, 5-15, and 17-18 Under Nonstatutory Obviousness-Type Double Patenting

The Examiner has provisionally rejected claims 1-3, 5-15, and 17-18 based on nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-9, 11-23, 25, and 26 of copending U.S. Appl. No. 11/077,550 to Shone *et al.* (Office Action, page 8, lines 8-10)[2]. Applicants respectfully traverse the rejection.

Applicants respectfully request that the currently asserted double patenting rejection be held in abeyance until claimed subject matter is otherwise deemed allowable. After analyzing the final allowed claim scope, Applicants will consider filing

[1] Applicants note that U.S. Appl. No. 11/644,010 has issued as U.S. Patent No. 7,607,384.

[2] Applicants note that U.S. Appl. No. 11/077,550 has been allowed and the issue fee paid January 6, 2010.

a terminal disclaimer if necessary to overcome any obviousness-type double patenting rejections.

V. Rejection of Claims 1-18, 24, and 26-30 Under Nonstatutory Obviousness-Type Double Patenting

The Examiner has rejected claims 1-18, 24, and 26-30 based on nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-8, 10-17, 20-29, 31, and 39-42 of copending U.S. Patent No. 7,192,596 to Shone *et al.* (Office Action, page 11, lines 8-10). Applicants respectfully traverse the rejection.

Applicants respectfully request that the currently asserted double patenting rejection be held in abeyance until claimed subject matter is otherwise deemed allowable. After analyzing the final allowed claim scope, Applicants will consider filing a terminal disclaimer if necessary to overcome any obviousness-type double patenting rejections.

VI. Objection to Claim 18

The Examiner has objected to claim 18 as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. (Office Action, page 16, lines 2-3). Applicants respectfully traverse the objection.

Claim 1 recites that the single chain polypeptide lacks a *functional* C-terminal part of a clostridial neurotoxin heavy chain designated H_C. Therefore, the single chain polypeptide of claim 1 may contain a C-terminal part of a clostridial neurotoxin heavy chain designated H_C as long as that C-terminal part is not functional.

Claim 18 is directed to a polypeptide according to claim 1, wherein said single chain polypeptide lacks a C-terminal part of a clostridial neurotoxin heavy chain designated H_C. Therefore, claim 18 further limits the subject matter of claim 1.

Accordingly, Applicants respectfully request that the objection to claim 18 be withdrawn.

VII. Objection to the Specification

The Examiner has objected to the specification as allegedly the citation to Kozaki *et al.* on page 3 is incomplete. (Office Action, page 16, lines 8-9).

The specification has been amended to correct the citation to Kozaki *et al.* No new matter has been added. Accordingly, Applicants respectfully request that the objection to the specification be withdrawn.

VIII. Rejection of Claims 1-30 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 1-30 under 35 U.S.C. § 112, first paragraph, as allegedly the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. (Office Action, page 16, lines 20-24). Applicants respectfully traverse the rejection.

The Examiner states that:

> To adequately describe the genus of a single chain polypeptide, Applicant must adequately describe both domains of clostridial neurotoxin light chain and SEQ ID NO:66 fragment/variant forms that are capable of cleaving vesicle or plasma membranes. Applicant must also describe the domain of clostridial neurotoxin heavy chain fragment/variant forms that

> are capable of translocating the polypeptide in the cell and increasing the solubility of the polypeptide.

(Office Action, page 17, lines 25-30). The Examiner further alleges that "[t]he specification, however, does not disclose distinguishing and identifying features of a representative number of members of the genus of a single chain polypeptide, to which the claims are drawn, such as a correlation between the structure of an isolated single chain polypeptide structure comprising fragments or variants of the domains, and its functions . . . so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus." (Office Action, page 18, lines 15-23). Applicants respectfully disagree.

The "descriptive text needed to meet these requirements [of written description] varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence." *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005). There is no need to re-describe what is already known. *See id.* A patent specification is written for one of skill in the art so "[a] claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language." *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1366 (Fed. Cir. 2006) (quoting *LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005)).

The Examiner is also reminded that the written description as filed is presumed to be adequate unless sufficient evidence has been presented by the Examiner to rebut the presumption. The Examiner has the burden of "presenting by a preponderance of

evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." MPEP § 2163.04.

The as-filed specification provides a detailed description of fragments and variants having the structural and functional features recited in the pending claims. As disclosed on pages 5-8 of the as-filed specification, the structure of clostridial neurotoxins and the function of their light chain and H_N domains was well-known prior to the filing of the present application. For example, Kurazano, H., *et al., J. Biol. Chem. 267*:14721-14729 (hereinafter "Kurazano") (cited on page 5 of the as-filed specification, attached herewith as Exhibit A), discloses the minimum domains necessary for cleavage activity (e.g. proteolytic enzyme activity) of a clostridial neurotoxin L-chain. The as-filed specification states that:

> Table II on page 14726 of Kurazano *et al.* (1992) illustrates a number of L-chain deletion mutants (both amino-terminal and carboxy-terminal L-chain deletion mutants are illustrated). Such mutants, together with other L-chain mutants containing, for example, similar amino acid deletions or conservative amino acid substitutions are embraced by the first domain definition of the present invention provided that the L-chain component in question has the requisite cleavage activity.

(page 5, lines 7-12 of the as-filed specification). Kurazano also discloses the structure of clostridial neurotoxin heavy chains, together with the functions associated with the H_N domain of the heavy chain (*see* Figure 1 on page 14722 of Kurazano).

The as-filed specification discloses that the sole requirement for a fragment or variant of the first domain is that it retains the cleavage function of a clostridial neurotoxin light chain (page 4, lines 27-28). The as-filed specification further discloses that a fragment of the first domain can be a "N-terminal, C-terminal fragment of the light chain, or is an internal fragment, so long as it substantially retains the ability to cleave

the vesicle or plasma-membrane associated protein essential to exocytosis" (page 12, lines 20-22). The as-filed specification also discloses that the variant of the first domain "has a different peptide sequence from the light chain or from the fragment, though it too is capable of cleaving the vesicle or plasma-membrane associated protein" (page 12, lines 23-24). The variant may differ from the reference sequence by way of one or more amino acid insertions, deletions, and/or substitutions. In some embodiments, the variant sequence may comprise an N-terminal extension, a C-terminal extension, and/or one or more amino acid alterations as compared to the sequence of a clostridial neurotoxin light chain (page 12, line 27, through page 13, line 3).

The as-filed specification discloses that the sole requirement for a fragment or variant of the second domain is that it retains the translocation and/or solubilizing activity of a clostridial neurotoxin heavy chain H_N (page 6, lines 23-25). The as-filed specification discloses that simple assays were available before the filing date of the application to determine whether a particular clostridial neurotoxin H_N portion (or equivalent H_N component) had the requisite translocation function (page 7, lines 5-7). The as-filed specification further provides written description for the fragments and variants of the second domain which are "conveniently obtained by insertion, deletion and/or substitution of a H_N domain or fragment thereof" (see page 13, lines 13-25).

The as-filed specification further discloses that:

> Prior to the present application a number of conventional, simple assays were available to allow a skilled person to routinely confirm whether a given L-chain (or equivalent L-chain component) had the requisite cleavage activity. These assays are based on the inherent ability of a functional L-chain to effect peptide cleavage of specific vesicle or plasma membrane associated proteins (eg. synaptobrevin, syntaxin, or SNAP-25) involved in neuronal exocytosis, and simply test for the presence of the cleaved product/s of said proteolytic reaction.

(page 5, lines 13-19). Conventional assays suitable for detecting clostridial neurotoxin H_N polypeptide translocation activity are described in Blaustein, R.O., *et al., FEBS 226*: 115-120 (1987)(attached herewith as Exhibit B) and Shone, C.C., *et al., Eur. J. Biochem. 167*:175-180 (1987)(attached herewith as Exhibit C).

The as-filed specification also discloses the preparation of the variant single-chain polypeptides shown in SEQ ID NOs: 2, 4, 10, 12, and 26 (Example 1, pages 62-68). These variants comprise multiple amino acid substitutions and/or insertions/extensions as compared with the amino acid sequence of the corresponding clostridial neurotoxin light chain and heavy chain H_N. Additionally, the expression of a variant single-chain polypeptide in *E. coli* is disclosed in Examples 4-9 of the as-filed specification (pages 71-75).

The as-filed specification also discloses the preparation of the single-chain variant and fragment polypeptides shown in SEQ ID NOs: 20, 22, and 24 (Example, 2, pages 68-69). These single-chain variant and fragment polypeptides contain deletions in the second domain as compared to the corresponding clostridial neurotoxin heavy chain H_N.

Although the Applicant could have disclosed additional representative members of the genus of single chain polypeptides, it was not necessary to do so, because it is not necessary to disclose what was already known in the art. Support for this conclusion is found in *Invitrogen Corporation v. Clontech Laboratories, Inc.*, 429 F.3d 1052 (Fed. Cir. 2005), in which the independent claim at issue recited "[a]n isolated polypeptide having polymerase activity and substantially reduced RNase H activity" *Id.* at 1072. In *Invitrogen*, Clontech argued that Invitrogen's claims were invalid for lack of written

description, because the claims were "not limited to sequences recited in the specification and do not recite DNA or protein sequences." *Id.* at 1073. The Federal Circuit rejected Clontech's argument, and explained that "the district court found it undisputed that in addition to the sequence recited in the specification at bar, 'at the time of the invention, the sequences of RT genes were known and members of the RT gene family shared significant homologies from one species of RT to another.'" *Id.* (quoting *Invitrogen Corp. v. Clontech Labs.*, Nos. AW-96-4080, AW-00-1879 (D.Md. October 17, 2003)). The Federal Circuit also rejected Clontech's argument that *University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Circ. 1997), compelled a conclusion that Invitrogen's claims were not described. *See id.* The Federal Circuit affirmed the district court's holding that Invitrogen's claims were not invalid for lack of written description. *See id.* at 1073-74.

Thus, under *Invitrogen*, it was not necessary to provide an exhaustive list of representative members in the present specification in order for the single chain polypeptide to be described, because, as discussed above, many representative members of the genus of single chain polypeptides were known in the art.

Applicants assert that the present specification provides sufficient written description to convey to one of ordinary skill that Applicants had possession of the full scope of the claimed invention upon filing the application. Therefore, Applicants respectfully request that the rejection of claims 1-30 under 35 U.S.C. § 112, first paragraph, be withdrawn.

IX. Rejection of Claims 1-30 Under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 1-30 under 35 U.S.C. § 112, first paragraph, as allegedly the specification while being enabling for a single chain polypeptide (first and second domain is clostridial neurotoxin light chain and clostridial neurotoxin heavy chain respectively), the single chain polypeptide comprising SEQ ID NO:66, does not reasonable provide enablement for a single chain polypeptide comprising fragments or variants thereof of the clostridial neurotoxin light chain or the clostridial neurotoxin heavy chain or SEQ ID NO:66. (Office Action, page 21, lines 13-18). Applicants respectfully traverse the rejection.

The Examiner alleges that:

> the claimed inventions are not enabled for a single chain polypeptide comprising fragments or variants thereof of the Clostridial neurotoxin light chain, or SEQ ID NO:66, nor a portion of Clostridial neurotoxin heavy chain. The claims encompassing all fragments and variants of clostridial neurotoxin light chain, clostridial neurotoxin heavy chain, and further fragments and variants of SEQ ID NO:66 is overly broad. It is not routine in the art to screen for positions within the protein's sequence wherein amino acid modifications (i.e. additions, deletions, or modifications) can be made with a reasonable expectation of success in obtaining similar activity/utility limited in any protein.

(Office Action, page 25, lines 19-26). Applicants respectfully disagree.

In order to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, the claimed invention must be enabled so that a person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance regarding the direction in which the experimentation should proceed. *Id.*

In the Declaration of Clifford Charles Shone[3] Under 37 CFR § 1.132 (attached herewith as Exhibit D), Dr. Shone discloses suitable tests for confirming clostridial neurotoxin light chain and clostridial neurotoxin heavy chain H_N function. In Annex 1 of the Declaration, Dr. Shone states that a number of routine methods for confirming that a particular clostridial neurotoxin L-chain (or fragment or variant thereof) has the requisite protease activity were known prior to the filing date of the present application. Dr. Shone lists the SNAP-25 test as an example of a simple assay disclosed in the as-filed specification (page 5, lines 13-19) that was available prior to the filing date of the present application (Annex 1 of the Declaration). Dr. Shone also states that protease activity can be monitored by disappearance of the L-chain substrate or by detecting protease cleavage products using an assay comprising antibodies as described in PCT/GB95/01279 (Annex 1 of the Declaration). In Annex 2 of the Declaration, Dr. Shone states that a number of routine methods for confirming that a fragment or variant polypeptide has the required H_N activity were known prior to the filing date of the present application. Dr. Shone states that the methods described by Blaustein, R.O., *et al., FEBS 226*: 115-120 (1987) and Shone, C.C., *et al., Eur. J. Biochem. 167*:175-180 (1987) are suitable (Annex 2 of the Declaration).

Therefore, a person of ordinary skill in the art would be familiar with simple, conventional tests for confirming whether a given polypeptide fragment or variant possesses the desired "first domain" function of cleaving one or more vesicle or plasma membrane associated proteins essential to exocytosis. A person of ordinary skill in the

[3] Clifford Charles Shone is an inventor of the above-captioned application and an employee of the Health Protection Agency, the assignee of the above-captioned application.

would also be familiar with simple, conventional tests for confirming whether a given polypeptide fragment or variant possesses the desired "second domain" function of translocating the polypeptide into a cell and/or increasing the solubility of the polypeptide.

Furthermore, Applicants submit that for product or composition claims, teaching how to make and use a single embodiment is sufficient to meet the enablement requirement, even for broad claims covering many species. In *Invitrogen Corp. v. Clontech Labs, Inc.*, 429 F.3d 1052 (Fed. Cir. 2005), the Federal Circuit, quoting the district court, stated that "[t]he enablement requirement is met if the description enables *any mode* of making and using the invention." 429 F.3d at 1071 (emphasis added). In *Invitrogen*, Clontech argued that the claims were not enabled because the specification allegedly failed to explain how to make the mutants using point mutations. *See id.* at 1070. The court rejected Clontech's argument, noting that the claims were not limited by the method of achieving the mutation. *See id.* at 1071. The court stated that "Invitrogen fully described an operable method for achieving the claimed invention." and held that the claims were not invalid for lack of an enabling disclosure. *Id.* Similarly, Applicants claim is directed to a product and is not limited by a method of using the product.

The Examiner states that "[i]n view of the lack of support in the art and specification, associated with regard to the single chain polypeptide as claimed and the changes which can be made in the single chain polypeptide structure to make it a fragment or variant of the domains and still maintain their function as claimed, it would require undue experimentation." (Office Action, page 25, line 27, through page 26, line 1). However, the art of record and the currently submitted evidence clearly establishes

otherwise. Applicants submit that the specification provides considerable direction and guidance on how to practice the claimed invention and presents examples of variants and fragments of the single chain polypeptide. Furthermore, Applicants submit that the methods to determine whether the fragment or variant has the required activity were well-known to those of ordinary skill in the art. Therefore, Applicants submit that based on the as-filed specification and the assays available as of the filing date of the present application, one of ordinary skill in the art could make and use a single chain polypeptide or fragment or variant thereof, without undue experimentation.

Accordingly, Applicants respectfully request that the rejection of claims 1-30 under 35 U.S.C. § 112, first paragraph, be withdrawn.

X. Rejection of Claims 1, 2, 3, 5, and 14 Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 1, 2, 3, 5, and 14 under 35 U.S.C. § 112, second paragraph, as allegedly the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. (Office Action, page 26, lines 7-9). Applicants respectfully traverse the rejection.

The Examiner states that claim 1 is indefinite in the recitation of the phrase "capable of." (Office Action, page 26, lines 10-11). In furtherance of prosecution, amended claim 1 does not contain the phrase "capable of."

The Examiner states that claims 1 and 5 recite the term "portion" which is allegedly not a recognized term and is not defined in the specification. (Office Action, page 26, lines 14-20). In furtherance of prosecution, amended claims 1 and 5 do not contain the term "portion."

The Examiner also states that claims 2, 3, 5, and 14 recite the limitation "clostridial toxin heavy chain" and there is insufficient antecedent basis for this limitation in claim 1. (Office Action, page 26, lines 21-23). In furtherance of prosecution, amended claims 2, 3, 5, and 14 do not contain the phrase "clostridial toxin heavy chain."

Accordingly, Applicants respectfully request that the rejection of claims 1, 2, 3, 5, and 14 under 35 U.S.C. § 112, second paragraph, be withdrawn.

XI. Rejection of Claims 1-18, 24, and 26-30 Under 35 U.S.C. § 102(e)

The Examiner has rejected claims 1-18, 24, and 26-30 under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 7,192,596 to Shone *et al.* (hereinafter "the '596 patent"). (Office Action, page 27, lines 11-12). Applicants respectfully traverse the rejection.

Claim 1 of the present application recites an isolated polypeptide, wherein said isolated polypeptide is a single chain polypeptide selected from the group consisting of a (I) single chain polypeptide comprising a sequence selected from the group consisting of SEQ ID NO: 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 139, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, and 175, (II) a fragment of the single chain polypeptide of (I), or (III) a variant of the single chain polypeptide of (I).

The present application claims priority to U.S. Patent Appl. No. 10/241,596, filed September 12, 2002. Therefore, the 102(e) date for the subject matter of the present application is September 12, 2002.

The '596 patent was filed on September 12, 2002, as U.S. Patent Appl. No. 10/241,596 (hereinafter "the '596 application") and is a continuation-in-part of U.S. Patent Appl. No. 09/255,829, filed February 23, 1999, which is a national stage of PCT/GB97/02273, filed August 22, 1997, which is a continuation-in-part of U.S. Appl. No. 08/782,893, filed December 27, 1996. The Sequence Identification Numbers recited in claim 1 of the present application were first disclosed in the '596 application, filed September 12, 2002.

Because the subject matter of the pending claims was not described in the '596 application "before the invention" of the present application, Applicants submit that the '596 patent is not prior art to the pending claims under 102(e). Applicants respectfully request that the rejection of claims 1-18, 24, and 26-30 under 35 U.S.C. § 102(e), be withdrawn.

XII. Rejection of Claims 1-3, 5-15, and 17-18 Under 35 U.S.C. § 102(e)

The Examiner has rejected claims 1-3, 5-15, and 17-18 under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent Appl. Publication No. 2005/0244435 to Shone *et al.* (hereinafter "the '435 publication")[4]. (Office Action, page 27, lines 19-20). Applicants respectfully traverse the rejection.

[4] U.S. Patent Appl. Publication No. 2005/0244435 corresponds to U.S. Appl. No. 11/077,550, which has been allowed and the issue fee paid.

Claim 1 of the present application recites an isolated polypeptide, wherein said isolated polypeptide is a single chain polypeptide selected from the group consisting of a (I) single chain polypeptide comprising a sequence selected from the group consisting of SEQ ID NO: 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 139, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, and 175, (II) a fragment of the single chain polypeptide of (I), or (III) a variant of the single chain polypeptide of (I).

The present application claims priority to U.S. Patent Appl. No. 10/241,596, filed September 12, 2002. Therefore, the 102(e) date for the subject matter of the present application is September 12, 2002.

The '435 publication was filed on March 11, 2005, as U.S. Patent Appl. No. 11/077,550 and is a continuation-in-part of the '596 application, filed September 12, 2002, which is a continuation-in-part of U.S. Patent Appl. No. 09/255,829, filed February 23, 1999, which is a national stage of PCT/GB97/02273, filed August 22, 1997, which is a continuation-in-part of U.S. Appl. No. 08/782,893, filed December 27, 1996. The Sequence Identification Numbers recited in claim 1 of the present application were first disclosed in the '596 application, filed September 12, 2002.

Because the subject matter of the pending claims was not described in the '435 publication "before the invention" of the present application, Applicants submit that the '435 publication is not prior art to the pending claims under 102(e). Applicants respectfully request that the rejection of claims 1-3, 5-15, and 17-18 under 35 U.S.C. § 102(e), be withdrawn.

Conclusion

Prompt and favorable consideration of this Amendment and Reply is respectfully requested. Applicants believe the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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